REMARKS

The Office Communication mailed August 13, 2008 indicates that the Amendment filed May 19, 2008 was entered. However, the Examiner asserts that newly added claims 76-79 are improperly dependent, based on their depending from canceled claims, and requires that these claims be amended.

In response, Applicants provide herewith an updated Listing of Claims, in which claims 77-79 have been amended to update the dependency for each. Applicants note that claim 76 presently depends from pending claim 2 and as such, is properly dependant. Accordingly, claim 76 has not been amended. Upon entry of the amendment, claims 2-4, 8, 11, 12, 27-29, 32-41, 68, and 76-79 will remain pending and under consideration.

The Examiner has further required, under 37 CFR 1.105, that Applicants submit the poster presented at the 43rd Annual Meeting of the American Society of Hematology on December 7-11, 2001, corresponding to the abstract already of record set forth in Cantwell *et al.*, *Blood* 98 Part 1, page 423a, 2001. Accordingly, the Cantwell *et al.* poster corresponding to the Cantwell *et al.* abstract is enclosed with the IDS submitted herewith, as requested. As can be seen from comparison of the documents, their content is identical.

Applicants also provide the following explanation with respect to the Examiner's comment that the Prussak Declaration does not appear to support the claims.

Dr. Prussak's declaration confirms that, as reported in the Cantwell *et al.* abstract, soluble TNF is released from (a) a TNF molecule lacking a metalloproteinase (mmp) cleavage site; and (b) is also released from a CD154/TNFα chimera (SEQ ID NO: 9) where the chimera possesses an intact mmp cleavage site (see also, specification at pages 35-36, paragraph 116). In particular, paragraphs 6-10 of the Declaration describe data demonstrating soluble TNF release from native TNF molecules lacking an mmp cleavage site (similar to those described in the Mueller *et al.*, *J Biol Chem* 274:38112, 1999) and from chimeric molecules where the mmp cleavage sites are present (as described in the Cantwell abstract).

In contrast, Dr. Prussak's declaration (paragraphs 11-14) also confirms that, as not recognized by the prior art, the best results - up to complete elimination of soluble TNF release - are provided by a chimeric molecule which lacks cleavage sites in the domains that comprise the CD154/TNFα junction (III and IV; SEQ ID NO: 1). Based on these data, and as reflected in the disclosure of the application, Dr. Prussak concludes that, to provide a membrane-stable TNF molecule with reduced soluble TNF release as claimed, a chimeric molecule lacking an mmp cleavage site is required (see, e.g., paragraphs 15 and 16). Thus, it is those molecules that are the subject of the present claims, whose distinction with respect to the prior art is therefore supported by Dr. Prussak's Declaration.

CONCLUSION

Applicants believe that the present application is now in condition for allowance. Favorable consideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

No fee is believed to be due in connection with filing this paper. However, the Commissioner is hereby authorized to charge any other fees associated with the filing submitted herewith, or credit any overpayments to Deposit Account No. 07-1896 referencing the above-identified attorney docket number.

Respectfully submitted,

Date: October 9, 2008

Stacy L. Taylor
Registration No. 34,842
Telephone: (858) 677-1423
Facsimile: (858) 677-1465

DLA PIPER US LLP
4365 Executive Drive, Suite 1100
San Diego, CA 92121-2133
USPTO Customer Number 28213